

July 2, 2001

Page 2 of 7

Form PTO-1449 U.S. Department of Commerce  
Patent and Trademark Office

Atty. Docket No.

Serial No.

54938-236531

09/864,685

Applicant

ZOLTAN KISS

Filing Date

Group

May 24, 2001

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

## U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
<i>FL</i>	4,564,675	1/14/86	Kurabayashi et al.			
	4,645,661	2/24/87	Schonbaum			
	4,745,109	5/17/88	Bednarski et al.			
	5,023,253	6/11/91	Remers et al.			
	5,686,436	11/11/97	Van Dyke			
	5,783,596	7/21/98	Medford et al.			
	5,856,353	1/5/99	Tung et al.			
	5,916,910	6/29/99	Lai			
	5,922,761	7/13/99	Lai			
	5,958,918	9/28/99	Ewing et al.			
<i>FL</i>	6,074,643	6/13/00	Barbera-Guillem			

## FOREIGN PATENT DOCUMENTS

Name	Document Number	Date	Country	Class	Subclass	Translation Yes/No
<i>FL</i>	WO 00/35930	22.06.00	PCT			Yes

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	See separately attached section entitled "Other Documents"

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Examiner: *Krass*Date Considered: *03/09/03*

July 2, 2001

Page 3 of 7

Form PTO-1449 U.S. Department of Commerce  
Patent and Trademark OfficeINFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

Atty. Docket No.	Serial No.
54938-236531	09/864,685
Applicant	
ZOLTAN KISS	
Filing Date	Group
May 24, 2001	

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

<del>FK</del>	Product Information, Kamiya Biomedical Company, 1 pg., undated.
	Burkitt, Mark J.; Bishop, Hugh S.; Milne, Lesley; Tsang, Shui Ying; Provan, Gordon J.; Nobel, C. Stefan I.; Orrenius, Sten; Slater, Andrew F. G., "Dithiocarbamate Toxicity toward Thymocytes Involves Their Copper-Catalyzed Conversion to Thiuram Disulfides, Which Oxidize Glutathione in a Redox Cycle without the Release of Reactive Oxygen Species," Archives of Biochemistry and Biophysics, 353, 73-84, 1998.
	Orrenius, S.; Nobel, C. S. I.; van den Dobbelsteen, M. J.; Burkitt, M. J.; Slater, A. F. G., "Dithiocarbamates and the redox regulation of cell death." Biochemical Society Transactions, 24, 1032-1038, 1996.
	Fürstenberger, G.; Amtmann, E.; Marks, F.; Sauer, G., "Tumor Prevention by a Xanthate Compound in Experimental Mouse-skin Tumorigenesis," Int. J. Cancer, 43, 508-512, 1989.
	Kim, Chul Hoon; Kim, Joo Hee; Xu, Jan; Hsu, Chung Y.; Ahn, Young Soo, "Pyrrolidine Dithiocarbamate Induces Bovine Cerebral Endothelial Cell Death by Increasing the Intracellular Zinc Level," Journal of Neurochemistry, 72, 1586-1592, 1999.
	Chinery, Rebecca; Brockman, Jeffrey A.; Peeler, Mark O.; Shyr, Yu; Beauchamp, R. Daniel; Coffey, Robert J., "Antioxidants enhance the cytotoxicity of chemotherapeutic agents in colorectal cancer: A p53-independent induction of p21 <sup>WAF1/CIP1</sup> via C/EBPβ," Nature Medicine, 3, 1233-1241, 1997.
	Nobel, C. Stefan I.; Kimland, Monica; Lind, Birger; Orrenius, Sten; Slater, Andrew F. G., "Dithiocarbamates Induce Apoptosis in Thymocytes by Raising the Intracellular Level of Redox-active Copper," The Journal of Biological Chemistry, 270, 26202-26208, 1995.
	Erl, Wolfgang; Weber, Christian; Hansson, Göran K., "Pyrrolidine dithiocarbamate-induced apoptosis depends on cell type, density, and the presence of Cu <sup>2+</sup> and Zn <sup>2+</sup> ," American Journal of Physiology, 278, C1116-C1125, 2000.
↓ FK	Chung, Kwang Chul; Park, Jae Hyun; Kim, Chul Hoon; Lee, Hyun Woo; Sato, Noboru; Uchiyama, Yasuo; Ahn, Young Soo, "Novel Biphasic Effect of Pyrrolidine Dithiocarbamate on Neuronal Cell Viability Is Mediated by the Differential Regulation of Intracellular Zinc and Copper Ion Levels, NF-kB, and MAP Kinases," Journal of Neuroscience Research, 59, 117-125, 2000.

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Examiner: KrassDate Considered: 03/09/03

July 2, 2001

Page 4 of 7

Form PTO-1449 U.S. Department of Commerce  
Patent and Trademark OfficeINFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

Atty. Docket No.	Serial No.
54938-236531	09/864,685
Applicant	
ZOLTAN KISS	
Filing Date	Group
May 24, 2001	

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Nobel, C. Stefan I., Burgess, David H.; Zhivotovsky, Boris; Burkitt, Mark J.; Orrenius, Sten; Slater, Andrew F. G., "Mechanism of Dithiocarbamate Inhibition of Apoptosis: Thiol Oxidation by Dithiocarbamate Disulfides Directly Inhibits Processing of the Caspase-3 Proenzyme," Chemical Research in Toxicology, 10, 636-643, 1997.
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	McCabe, Jr., Michael J.; Jiang, Shun Ai; Orrenius, Sten, "Chelation of Intracellular Zinc Triggers Apoptosis in Mature Thymocytes," Laboratory Investigation, 69, 101-110, 1993.
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Tsai, Jer-Chia; Jain, Mukesh; Hsieh, Chung-Ming; Lee, Wen-Sen; Yoshizumi, Masao; Patterson, Cam; Perrella, Mark A.; Cooke, Carol; Wang, Hong; Haber, Edgar; Schlegel, Robert; Lee, Mu-En, "Induction of Apoptosis by Pyrrolidinedithiocarbamate and N-Acetylcysteine in Vascular Smooth Muscle Cells," The Journal of Biological Chemistry, 271, 3667-3670, 1996.
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Ragione, Fulvio Della; Cucciolla, Valeria; Borriello, Adriana; Pietra, Valentina Della; Manna, Caterina; Galletti, Patrizia; Zappia, Vincenzo, "Pyrrolidine Dithiocarbamate Induces Apoptosis by a Cytochrome c-Dependent Mechanism," Biochemical and Biophysical Research Communications, 268, 942-946, 2000.
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Kiss, Zoltan; Crilly, Karan S.; Chung, Taeowan, "Stimulation of DNA Synthesis in Untransformed Cells by the Antiviral and Antitumoral Compound Tricyclodecan-9-yl-xanthogenate (D609)," Biochemical Pharmacology, 55, 915-918, 1998.
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Amtmann, Eberhard; Müller, Karin; Knapp, Anita; Sauer, Gerhard, "Reversion of Bovine Papillomavirus-induced Transformation and Immortalization by a Xanthate Compound," Experimental Cell Research, 161, 541-550, 1985.
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Sauer, Gerhard; Amtmann, Eberhard; Melber, Karl; Knapp, Anita; Müller, Karin; Hummell, Klaus; Scherm, Arthur, "DNA and RNA virus species are inhibited by xanthates, a class of antiviral compounds with unique properties," Proc. Natl. Acad. Sci. USA, 81, 3263-3267, 1984.
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Chirney, Rebecca; Beauchamp, R. Daniel; Shyr, Yu; Kirkland, Susan C.; Coffey, Robert J.; Morrow, Jason D., "Antioxidants Reduce Cyclooxygenase-2 Expression, Prostaglandin Production, and Proliferation in Colorectal Cancer Cells <sup>1</sup> ," Cancer Research, 58, 2323-2327, 1998.
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Waxman, David J., "Glutathione S-Transferases: Role in Alkylating Agent Resistance and Possible Target for Modulation Chemotherapy-A Review <sup>1</sup> ," Cancer Research, 50, 6449-6454, 1990.

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Examiner: Krass

Date considered: 03/09/03

July 2, 2001

Page 5 of 7

Form PTO-1449 U.S. Department of Commerce  
Patent and Trademark Office

Atty. Docket No.

Serial No.

54938-236531

09/864,685

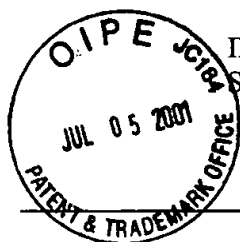
Applicant

ZOLTAN KISS

Filing Date

Group

May 24, 2001

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

FL		Ploemen, Jan H. T. M.; van Ommen, Ben; van Bladeren, Peter J.; "Inhibition of Rat and Human Glutathione S-Transferase Isoenzymes by Ethacrynic Acid and its Glutathione Conjugate," Biochemical Pharmacology, 40, 1631-1635, 1990.
		Ciaccio, Paul J.; Tew, Kenneth D.; LaCreta, Frank P., "Enzymatic conjugation of chlorambucil with glutathione by human glutathione S-transferases and inhibition by ethacrynic acid," Biochemical Pharmacology, 42, 1504-1507, 1991.
		Tew, Kenneth D.; Bomber, Annette M.; Hoffman, Sandra J., "Ethacrynic Acid and Piriprost as Enhancers of Cytotoxicity in Drug Resistant and Sensitive Cell Lines <sup>1</sup> ," Cancer Research, 48, 3622-3625, 1988.
		O'Dwyer, Peter J.; LaCreta, Frank; Nash, Sherri; Tinsley, Peter W.; Schilder, Russell; Clapper, Margie L.; Tew, Kenneth D.; Panting, Lisa; Litwin, Samuel; Comis, Robert L.; Ozols, Robert F., "Phase I Study of Thiotepe in Combination with the Glutathione Transferase Inhibitor Ethacrynic Acid <sup>1</sup> ," Cancer Research, 51, 6059-6065, 1991.
		LaCreta, Frank P.; Brennan, James M.; Nash, Sherrie L.; Comis, Robert L.; Tew, Kenneth D., O'Dwyer, Peter J., "Pharmacokinetics and Bioavailability Study of Ethacrynic Acid as a Modulator of Drug Resistance in Patients with Cancer <sup>1</sup> ," The Journal of Pharmacology and Experimental Therapeutics, 270, 1186-1191, 1994.
		Kang, Y. James, "Buthionine Sulfoximine Enhances Glutathione-But Attenuates Glutamate-Stimulated Cell Proliferation," Cellular and Molecular Biology Research, 41, 131-136, 1995.
		Liebmann, James E.; Hahn, Stephen M.; Cook, John A.; Lipschultz, Claudia; Mitchell, James B.; Kaufman, Dwight C., "Glutathione Depletion by L-Buthionine Sulfoximine Antagonizes Taxol Cytotoxicity," Cancer Research, 53, 2066-2070, 1993.
		Malewicz, Barbara; Mukherjee, Jagot J.; Crilly, Karan S.; Baumann, Wolfgang J.; Kiss, Zoltan, "Phosphorylation of ethanolamine, methylethanolamine, and dimethyl-ethanolamine by overexpressed ethanolamine kinase in NIH 3T3 cells decreases the co-mitogenic effects of ethanolamines and promotes cell survival," Eur. J. Biochem., 253, 10-19, 1998.
FL		Schreck, Ralf; Meier, Beate; Männel, Daniela N.; Dröge, Wulf; Baeuerle, Patrick A., "Dithiocarbamates as Potent Inhibitors of Nuclear Factor kB Activation in Intact Cells," The Journal of Experimental Medicine, 178, 1181-1194, 1992.

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Examiner: Krass

Date Considered: 03/09/09

July 2, 2001

Page 6 of 7

Form PTO-1449 U.S. Department of Commerce  
Patent and Trademark OfficeINFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

Atty. Docket No.

Serial No.

54938-236531

09/864,685

Applicant

ZOLTAN KISS

Filing Date

Group

May 24, 2001

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

<i>fr</i>		Kastan, Michael B. "To oxidize or not to oxidize?" Nature Medicine, 3, 1192-1193, 1997.
<i> </i>		Chinery, Rebecca; ; Beauchamp, R. Daniel; Shyr, Yu; Kirkland, Susan C.; Coffey, Robert J.; Morrow, Jason D., "Antioxidants Reduce Cyclooxygenase-2 Expression, Prostaglandin Production, and Proliferation in Colorectal Cancer Cells," Cancer Research, 58, 2323-2327, 1998.
<i> </i>		Brennan, Paul; O'Neill, Luke A. J., "2-Mercaptoethanol restores the ability of nuclear factor $\kappa$ B (NF $\kappa$ B) to bind DNA in nuclear extracts from interleukin 1-treated cells incubated with pyrrolidine dithiocarbamate (PDTTC)," Biochemical Journal, 320, 975-981, 1996.
<i> </i>		Wu, Min; Lee, Hayyoung; Bellas, Robert E.; Schauer, Stephanie L.; Arsura, Marcello; Katz, David; FitzGerald, Mark J.; Rothstein, Thomas L.; Sherr, David H.; Sonenshein, Gail E., "Inhibition of NF- $\kappa$ B/Rel induces apoptosis of murine B cells," The Embo Journal, 15, 4682-4690, 1996.
<i> </i>		Trombetta, Louis D.; Toulon, Maureen; Jamall, I. Siraj, "Protective Effects of Glutathione on Diethyldithiocarbamate (DDC) Cytotoxicity: A Possible Mechanism," Toxicology and Applied Pharmacology, 93, 154-164, 1988.
<i> </i>		Halstead, Jennifer; Kemp, Kathleen; Ignatz, Ronald A., "Evidence for Involvement of Phosphatidylcholine-Phospholipase C and Protein Kinase C in Transforming Growth Factor- $\beta$ Signaling," The Journal of Biological Chemistry, 270, 13600-13603, 1995.
<i> </i>		Schenk, H.; Klein, M.; Erdbrugger, W.; Droge, W.; Schulze-Osthoff, K., "Distinct Effects of Thioredoxin and Antioxidants on the Activation of Transcription Factors NF- $\kappa$ B and AP-1," Proc. Natl. Acad. Sci. USA, 91, 1672-1676, 1994.
<i> </i>		Lees, G.J.; Cuajungco, M.P., Leong, W., "Effect of metal chelating agents on the direct and seizure-related neuronal death induced by zinc and kainic acid," Brain Research, 13, 108-117, 1998.
<i>fr</i>		Koh, Jae-Young; Suh, Sang W.; Gwag, Byoung J.; He, Yong Y.; Hsu, Chung Y.; Choi, Dennis W., "The Role of Zinc in Selective Neuronal Death After Transient Global Cerebral Ischemia," Science, 272, 1013-1016, 1996.

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

*Examiner: Krass**Date Considered: 03/07/03*

July 2, 2001  
Page 7 of 7

Form PTO-1449 U.S. Department of Commerce  
Patent and Trademark Office

Atty. Docket No.

Serial No.

54938-236531

09/864,685

Applicant

ZOLTAN KISS

Filing Date

Group

May 24, 2001

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT



OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

FR		Glassman, Armand B.; Rydzewski, Raymond S.; Bennett, Carol E., "Trace Metal Levels in Commercially Prepared Tissue Culture Media," Tissue and Cell, 12, 613-617, 1980.
		Schütze, Stefan; Potthoff, Karin; Machleidt, Thomas; Berkovic, Dinko; Wiegmann, Katja; Krönke, Martin, "TNF Activates NF-kB by Phosphatidylcholine-Specific Phospholipase C-Induced "Acidic" Sphingomyelin Breakdown," Cell, 71, 765-776, 1992.
		Müller-Decker, Karin; Doppler, Clemens; Amtmann, Eberhard; Sauer, Gerhard, "Interruption of Growth Signal Transduction by an Antiviral and Antitumoral Xanthate Compound," Experimental Cell Research, 177, 295-302, 1988.
↓ AK		Moellering, Douglas; McAndrew, Joanne; Hanjoong, Jo; Darley-USmar, Victor M., "Effects of Pyrrolidine Dithiocarbamate on Endothelial Cells: Protection Against Oxidative Stress," Free Radical Biology & Medicine, 26, 1138-1145, 1999.

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

M2:M2:20395786.01

Examiner: Krass

Date Considered: 03/09/03

